**BACKGROUND**

- Pain and other local injection-site reactions (SRS), including pruritus and erythema, are common with injectable sclerosis (MS) medications.
- SRS are responsible for non-adherence, poor sleep, anxiety, needle phobia and depression and are among the most common reasons for discontinuation of therapy for interferon beta (IFN) and the most common reason for discontinuation of glatiramer acetate (GA).
- Relieving injection-site pain may improve the tolerability of MS medications.
- SINERA® is a patented stick-topical adhesive (S-TA) with a novel heating component designed to enhance the delivery of an anesthetic mixture of lidocaine 10mg and tetracaine 7mg. S-TA has a controlled heat-assisted drug delivery (CHADD) system to warm the skin and facilitate drug delivery. This adhesive is approved in the USA for use in dermal analgesia and superficial dermatological procedures and may be used, in addition to reducing MS drug injection pain and needle phobia.

**OBJECTIVE**

To assess the effect of S-TA on immediate pain and other outcomes of discomfort with SC MS drug injection and to determine the preferred period of application (30 vs. 60 minutes) prior to injection.

**METHODS**

- This was an open-label, uncontrolled trial with pre- and post-treatment of one MS cohort with two active periods: 5-min S-TA application for 30 minutes before each injection. S-TA was to be removed immediately before injection (Figure 2).
- The duration of each treatment period was determined by the patient’s injectable medication
- Secondary efficacy measures included the following patient-reported outcomes, which were all performed at baseline and end of both study periods:
  - Pain at 12 hrs post-injection (0-10 VAS)
  - Pain at 24 hrs post-injection (0-10 VAS)
  - Fear of injection (0-10 VAS, recorded immediately before each injection)
  - Local Injection Site Reaction (LISR) scale (0-4, 0 = no reaction, see note)*
  - Injection site tenderness (0-10 VAS)
  - Global Impression of level of comfort with injections
- Statistical analyses were performed using Students’ t-test (P ≤ 0.05) or an equivalent non-parametric test. Null Hypothesis: Change mean or median = 0.

**RESULTS**

- There were 7 screen failures. (Low pain level ≤ 5, withdrew consent = 1, no diary = 1)
- A total of 30 patients were enrolled. There was 1 early termination (on GA 20mg).
- Twenty-nine patients completed (GA = 25, IFN = 4). See Table 2.

**TABLE 2. DEMOGRAPHIC AND BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total</th>
<th>Complete Patient</th>
<th>Completed Patients</th>
<th>No. Screened</th>
<th>Completed N</th>
<th>Study Completers</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQ)</td>
<td>49 (42-58)</td>
<td>48 (42-58)</td>
<td>48 (42-58)</td>
<td>50</td>
<td>48</td>
<td>48</td>
<td>48</td>
</tr>
</tbody>
</table>

**TABLE 3. INJECTION RELATED PATIENT REPORTED OUTCOMES**

<table>
<thead>
<tr>
<th>Pain at 12 hrs post-injection</th>
<th>S-TA 30 minutes</th>
<th>S-TA 60 minutes</th>
<th>Mean ± SD</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at 24 hrs post-injection</td>
<td>S-TA 30 minutes</td>
<td>S-TA 60 minutes</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Fear of injection (0-10 VAS)</td>
<td>S-TA 30 minutes</td>
<td>S-TA 60 minutes</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Local Injection Site Reaction Scale (0-4)</td>
<td>S-TA 30 minutes</td>
<td>S-TA 60 minutes</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
</tbody>
</table>

**FIGURE 3. STUDY DESIGN**

- 28 patients were randomized to one of five groups with 5-mm choosing one of the following periods: 30, 60, 90, 120, or 180 minutes before injection (Table 1).
- 120 patients were enrolled in the study.

**ADVERSE EVENTS (AE)**

- Two treatment-related adverse events were reported: allergic reaction involving muscle spasms and lightheadedness (N=1, moderate AE, subject on GA) and dermatitis (N=1, mild AE, subject on GA).

**DISCUSSION**

Significant reductions in pain were found only with both 30- and 60-minute applications of S-TA. The difference between the two applications was not significant.

Significant reductions in pain at 12 hours, pain at 24 hours, tenderness at 24 hours and Local Injection Site Reaction (LISR) scale score (93% of 24 were found with both 30- and 60-minute applications of S-TA).

There were no significant differences between 30- and 60-minute applications for these outcomes.

Fear of injection (FOI) was significantly less with S-TA for 30 minutes than for 60 minutes, possibly related to a period effect.

Global impression of level of comfort with injections was best for ST A-60 minutes application.

The difference was significant at baseline (p ≤ 0.01), but not vs. ST A-30 minute application (p > 0.1).

Subgroup analysis showed very similar results for GA group (N=25) and number was insufficient (N=6) for IFN group.

**LIMITATIONS**

- This was an uncontrolled, open-label trial. Subject numbers were small, especially for patients on interferon. Patient effects could not be excluded.

**CONCLUSIONS**

This pilot study explored the clinical utility of a topical adhesive (S-TA) containing anaesthetic and heating components in managing subcutaneous medicated injections used for MS treatment.

S-TA applied for 30 or 60 minutes prior to subcutaneous drug injection significantly reduced pain in injection, pain at 12 hours, pain, tenderness and LISR at 24 hours, and fear of injection. Pain reductions were seen with both 30- and 60-minute application of S-TA, suggesting that the shorter application time may be adequate.

Our findings support further study to establish the utility of this novel approach to treat injection pain caused by subcutaneous MS drug injections.

**REFERENCES**


**ACKNOWLEDGMENTS**

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